Remarks

Claims 34-45 are pending in the application. Claim 37 is withdrawn from consideration. Claim 34 has been amended, and support for this amendment can be found in the Appendix that was originally filed with the specification. Applicant submits that no new matter is introduced by the present Amendment.

All claims were previously rejected under 35 U.S.C. § 112, under 35 U.S.C. § 103, and for obviousness-type double patenting. The rejections under 35 U.S.C. § 112 are maintained. The prior rejections under 35 U.S.C. § 103 have apparently been removed. The double-patenting rejection remains, but is a provisional rejection and Applicant has previously indicated that no further comment will be provided until such time as an actual rejection is levied.

Rejection under 35 U.S.C. § 103(a) for allegedly being obvious

The Office Action also contains two "new" rejections under 35 U.S.C. § 103. The "new" § 103 rejections differ from prior § 103 rejections only in that additional secondary references have been added to the combination. These § 103 rejections are identical to the § 103 rejections in a related case, U.S.S.N. 10/728,051 ("the '051 application"). A response to a Final Office Action in the '051 application was submitted to the Patent Office on October 16, 2008. The § 103 arguments set forth in the response filed in the '051 application also apply to the present case and are reiterated below.

In Applicant's previous Response submitted on February 29, 2008, Applicant explained the many reasons that the base reference (WO 99/38978; "the '978 publication") cannot teach or suggest the claimed invention, whether alone or in combination with various cited references. None of these arguments is addressed, or even acknowledged, in the Office Action. As discussed below, Applicant submits that the Office Action is defective and should be withdrawn for this reason alone.

Moreover, Applicant points out that the "new" combinations cited by the Examiner do nothing to solve the previously-addressed deficiencies of the '978 publication, alone or in combination with the various secondary references. Indeed, the "new" combinations in fact represent a re-sorting of old combinations, with the further addition of yet more secondary references that are not even asserted to disclose core features of the present claims.

To be absolutely direct, the '978 publication, whether alone or in combination with any of the cited references, does not teach or suggest a modified allergen "encapsulated inside" dead *E. coli*, as recited in the present claims. Furthermore, the '978 publication does not teach or suggest any *pharmaceutical composition* comprising encapsulated modified allergens, as recited in the present claims. Indeed, as has been extensively discussed, several of the secondary references *teach explicitly away* from the claimed invention. To give but one example, some secondary references *require live* bacteria. There is absolutely no combination of these cited references that could teach or suggest the claimed invention.

The *sole* statement made by the Examiner with regard to "encapsulated inside" is that urea is used to solubilize a protein produced in the '978 publication. This statement is wholly irrelevant to the present claims.

First, the protein being solubilized with urea in the '978 publication is *not* a modified peanut allergen as recited in the present claims. That is, the '978 publication is describing urea purification of a *different protein*.

Second, the fact that the '978 inventors used urea in purifying a protein does not mean that the protein is "encapsulated within" bacteria.

Third, clearly, if the '978 inventors are isolating protein *from* dead *E. coli*, they are not preparing the dead *E. coli* as a *pharmaceutical composition*, as recited in the present claims.

For all of these reasons, the '978 publication cannot teach or suggest *pharmaceutical compositions* of *modified* allergens *encapsulated inside* dead *E. coli*. The Examiner cannot continue to ignore these points.

No list of secondary references, however long, is meaningful unless the cited secondary references in fact address the deficiencies of the primary reference. Moreover, the Examiner must take the teachings of the secondary references *as a whole* and may not ignore those portions that inconveniently teach away from the Examiner's intended combination, or from the claimed invention.

The "new" rejections levied in the Office Action add nothing substantive to the previously-levied rejections, yet the Office Action has not a single remark addressing, or even acknowledging, Applicant's prior arguments or amendments made in the Response submitted on

February 29, 2008. The Manual of Patent Examining Procedures ("MPEP") requires more. Indeed, the MPEP states, "Where the applicant traverses any rejection, the examiner should, if he or she repeats the rejection, *take note of the applicant's argument and answer the substance of it*." MPEP § 701.07(f) (emphasis added). Further, in the form paragraphs provided for Examiners use in establishing that "Arguments Are Not Persuasive" in an Office Action, the MPEP states, "The *examiner must address all arguments* which have not already been responded to in the statement of the rejection." MPEP § 7.37 (emphasis added). In the present case, the Examiner did not respond to a *single one* of Applicant's § 103 arguments from the February 29, 2008 Response, or even acknowledge that they *existed*.

Applicant recognizes that, on page 19 of the Office Action, the Examiner addresses some of Applicant's arguments that were made in an Office Action Response submitted almost two years ago (*i.e.*, on November 3, 2006). Applicant respectfully submits that the Examiner's statements appear to have been inadvertently carried over from a previous Office Action and *do not* address Applicant's arguments from the February 29, 2008 Response. Indeed, the Examiner addresses arguments made by Applicant in the November 3, 2006 Response to address a rejection under § 103 that (1) is *different* from the present § 103 rejections and (2) has *already been removed* by the Examiner. The Examiner did not address any of Applicant's arguments from the February 29, 2008 Response.

For all of these reasons, Applicant submits that the § 103 rejections levied in the Office Action are improper and should be removed. The present claims are not obvious over the cited art and are allowable.

Rejection under 35 U.S.C. § 112 for alleged lack of enablement and written description

The Examiner has rejected claims 34-36 and 38-47 for alleged lack of enablement and written description. In particular, the Examiner states that the specification does not provide written description for a composition comprising dead *E. coli* comprising *any* modified allergen.

As an initial matter, Applicant thanks the Examiner for entering into the record the substitute specification, which included material from U.S.S.N. 09/141,220 (the '220 application) that was incorporated by reference. As discussed during an interview between the Examiner and the Applicant that took place on August 27, 2007, and as set forth in Applicant's

previous Response submitted on February 29, 2008, the present specification, including the material from the '220 application, provides ample enablement and written description for the claims.

The § 112 rejections levied in the Office Action are virtually identical to the previously-levied rejections, yet the Office Action has not a single remark addressing, or even acknowledging, Applicant's prior arguments or amendments made in the Response submitted on February 29, 2008. As mentioned above in the discussion of the § 103 rejections, "The *examiner must address all arguments* which have not already been responded to in the statement of the rejection." MPEP § 7.37 (emphasis added). In the present case, the Examiner did not respond to a *single one* of Applicant's § 112 arguments from the February 29, 2008 Response, or even acknowledge that they *existed*.

Applicant reiterates the arguments made in the previous Response here. Applicant points out that the present specification includes the entire sequence of each of the wild type peanut allergens referred to in the claims (see, for example, SEQ ID NOs.: 2, 4, and 6); the specification also identifies or refers to the *known* IgE epitopes of each of these allergens (Tables 1-3 of the present specification). The specification also describes specific modifications of many of these IgE epitopes that reduce IgE binding (Tables 4-6 of the present specification). It is true that the specification does not specifically exemplify every possible mutation of every IgE epitope that can reduce IgE binding or cross-linking activity. However, as discussed during the interview, in light of the power of Molecular Biology, it is well within the purview of the person of ordinary skill to make other changes within these *precisely defined* sequences and to test them to assess their effects on IgE binding or cross-linking. Such work is routine, even if laborious. Certainly, it the experimentation it requires is no more *undue* than that required in *In re Wands*, the legal standard for enablement.

As mentioned in Applicant's previous Response, the specification includes an appendix including an extensive list of various wild type allergens of many different types (*e.g.*, weed pollens, grass pollens, tree pollens, mites, animals, fungi, insects, foods, among others). All of the listed allergens (~325 different allergens) include either GenBank accession numbers or references to published literature that describe these sequences. As discussed during the Interview, one of ordinary skill in the art reading the specification would easily be able to apply

the methods and principles explicitly exemplified in the specification to any of the ~325 allergens in the appendix.

In addition, as discussed above, the specification goes into great detail characterizing three of these allergens (*i.e.*, Ara h 1, Ara h 2, and Ara h 3). Although these three proteins are all peanut allergens with *names* that sound similar to one another, they are in fact three very *different* proteins with *different* amino acid sequences (SEQ ID NOs: 2, 4, and 6). Thus, the specification *describes and reduces to practice compositions and methods relating to three distinct proteins.* For all of these reasons, Applicant respectfully submits that the specification is enabling and fully descriptive for *any* allergen.

The Examiner states that the specification does not provide written description for a composition comprising dead *E. coli* comprising *any* modified allergen. For all of the reasons stated in Applicant's previous Response of February 29, 2008, Applicant does not agree with the Examiner's position. However, *solely* in order to further prosecution, and in spite of the fact that the Examiner failed to address any of Applicant's § 112 arguments from the previous Response, Applicant has amended claim 34 to recite the list of allergens presented in the Appendix that was originally filed with the present specification. Applicant respectfully submits that the specification *certainly* describes and enables a composition comprising an allergen selected from this group.

Conclusion

Applicant, therefore, respectfully submits that the present case is in condition for allowance. A Notice to that effect is respectfully requested.

If, at any time, it appears that a phone discussion would be helpful, the undersigned would greatly appreciate the opportunity to discuss such issues at the Examiner's convenience. The undersigned can be contacted at (617) 248-5175.

Please charge any fees that may be required for the processing of this Response, or credit any overpayments, to our Deposit Account No. 03-1721.

Respectfully submitted,

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